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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/812,862	03/20/2001	Jack R. Wands	00786-282003	2989

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FISH & RICHARDSON PC
225 FRANKLIN ST
BOSTON, MA 02110

EXAMINER	
VOGEL, NANCY S	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/812,862	WANDS ET AL.	
	Examiner	Art Unit	
	Nancy T. Vogel	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-11,13-17 and 19-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-11,13-17,19,21 and 26-37* is/are rejected.

7)☒ Claim(s) *20, 22-25* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-5, 7-11, 13-17, 19-37 are pending in the case.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The following are new rejections necessitated by applicant's amendments to the claims.

Claim Rejections - 35 USC § 102

Claims 26, 28, and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Birnbaum et al. (J. Virol. 64, 7, 3319-3330 (1990)).

Birnbaum et al. disclose nucleic acid encoding a polypeptide consisting of an amino acid sequence identical to a fragment of SEQ ID NO:12, wherein the carboxyterminal amino acid of the polypeptide corresponds to amino acids number 138, 139, 144, 149, or 164, thus falling within the range recited in the claims. The reference discloses vectors and host cells comprising said nucleic acids. (see Fig. 1 and page 3320).

Claims 26-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Beams et al. (previously cited).

Beams et al. disclose nucleic acids encoding a polypeptide comprising the HBV core protein having a carboxyterminus at amino acid 176 of SEQ ID NO: 12. Beams et

al. disclose vectors comprising said nucleic acids and cells comprising said vectors (see abstract, see page 600, first column line 17-28).

Claim Rejections - 35 USC § 103

Claims 1, 2, 7, 8, 13, 14, 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beams et al. (Virology 194:597-607) in view of Xian-Jun et al. (Hepatology, Vol. 1 No. 5, pp. 781-787 (1989)).

Beams et al. disclose a nucleic acid encoding a polypeptide that comprises a first amino acid sequence of at least 70 amino acids in length that is identical to a region of a wild type HBV core protein, and which lacks a second amino acid sequence of the wild type HBV core protein, wherein the second sequence comprises the carboxyterminal three amino acids of the wild type HBV core protein and does not exceed nine amino acids in length (see Fig. 1A, deletion of 7 carboxyterminal amino acids, designated Cd176). The reference discloses vectors containing said nucleic acid and cells containing said vectors (see page 600, first column line 17-28).

The difference between the reference and the instant claims is that different promoters are utilized.

However, Xian-Jun et al. disclose the use of hepatocyte- specific (i.e. those promoters normally associated with the genes encoding albumin, alpha-fetoprotein, alpha-antitrypsin, and retinal-binding protein), cytomegalovirus, herpes simplex virus, hepatitis virus, Rous sarcoma virus and SV40 virus promoters, all of which are disclosed to be active in hepatocyte cells, the cells known to be infected by HBV (see

page 781). It would have been obvious to one of ordinary skill in the art to have substituted any known promoter, such as those disclosed by Xian-Jun et al., in the vectors disclosed by Beams et al., since both references disclose the use of promoters for the expression of foreign genes, and the use of promoters known to be effective in hepatocytes would have been obvious to one of ordinary skill in the art who wished to express HBV genes, since HBV is known to infect hepatocyte cells. One would have been motivated to make this substitution by the desire to express recombinant HBV proteins in hepatocytes, since these are the cells normally infected by HBV.

Regarding the rejection of claims as being anticipated by Beams et al. in the previous Office action, applicants have argued that the amendment to the rejected claims has overcome this rejection since Beames does not disclose the nucleic acids that encode mutant hepadnaviral core proteins operably linked to one of the promoters recited in amended claim 1. However, the addition of the reference by Xian-Jun et al., in the newly presented rejection above, necessitated by applicant's amendment to the claims, overcomes applicant's arguments.

Claims 32-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Souw et al. in view of Beams et al. (both previously cited).

Souw et al. disclose nucleic acids encoding fusion polypeptides that comprise a first amino acid sequence of at least 70 amino acids in length that is identical to a region of a wild type hepadnavirus core protein, including one variant, delta 8, that has a deletion near the carboxyterminal end of the wild type hepadnavirus core protein, and

which comprise an amino acid sequence that is identical to a portion of a wild type hepadnavirus surface protein, vectors containing said nucleic acids, and cells containing said nucleic acids (see abstract and page 21 lines 3-24).

The reference does not disclose said nucleic acid in which the first amino acid mentioned above has an carboxyterminal amino acid corresponding to any of amino acids between positions 71 to 176 or between 178 to 180 of SEQ ID NO: 12 .

Beams et al. disclose a nucleic acid encoding a polypeptide that comprises a identical to a region of a wild type HBV core protein wherein the carboxyterminal end is at amino acid 176 of SEQ ID NO: 12 (see Fig. 1A, deletion of 7 carboxyterminal amino acids, designated Cd176). The reference discloses vectors containing said nucleic acid and cells containing said vectors (see page 600 first column line 17-28).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the nucleic acid disclosed by Souw et al. to include as the core protein element, the deletion mutants disclosed by Beams et al. having a carboxyterminal amino acid at position 176, in the disclosed fusion protein, and to further include the nucleic acid in a vector, and in a cultured cell, since Souw et al. disclose that any hepadnavirus (e.g. HBV) core protein variant, including fragments thereof, may be present in the disclosed fusion proteins.

One would have been motivated to include carboxyterminal deletions of the HBV core protein in the fusion proteins disclosed by Beams by the desire to express HBV antigens for the prevention or treatment of hepatitis or other undesirable consequences of HBV infection. The general teaching of any fragment or deletion of HBV core protein

fused to a HBV surface protein is disclosed in the Souw et al. reference, and therefore was well known in the art.

Claims 3-5, 9-11, 15-17, 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Souw et al. in view of Beams et al. (both previously cited) and Xian-Jun et al. (Hepatology, Vol. 1 No. 5, pp. 781-787 (1989)).

Souw et al. and Beams et al. are cited for the reasons made of record in the previous Office action, pages 6-7.

The difference between the references and the instant claims is that different promoters are utilized.

However, Xian-Jun et al. disclose the use of hepatocyte- specific (i.e. those promoters normally associated with the genes encoding albumin, alpha-fetoprotein, alpha-antitrypsin, and retinal-binding protein), cytomegalovirus, herpes simplex virus, hepatitis virus, Rous sarcoma virus and SV40 virus promoters, all of which are disclosed to be active in hepatocyte cells, the cells known to be infected by HBV (see page 781). It would have been obvious to one of ordinary skill in the art to have substituted any known promoter, such as those disclosed by Xian-Jun et al., in the vectors disclosed by Beams et al., since both references disclose the use of promoters for the expression of foreign genes, and the use of promoters known to be effective in hepatocytes would have been obvious to one of ordinary skill in the art who wished to express HBV genes, since HBV is known to infect hepatocyte cells. One would have

been motivated to make this substitution by the desire to express recombinant HBV proteins in hepatocytes, since these are the cells infected by HBV.

In their remarks submitted 3/26/03, Applicants have presented arguments regarding the rejection of the previously presented claims over Souw et al. in view of Beams et al. Applicants have argued that Beames does not provide the information missing in Souw, since Beames does not disclose or suggest the nucleic acids recited in claim 3, i.e. nucleic acids encoding core-surface protein fusion proteins linked to one of the promoters recited in claim 3. The promoters have been added to the claim in the amendment of 3/26/03, and the reference by Xian-Jun et al. teach these promoters, as set forth above. Furthermore, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. Although neither of the Souw or Beams references disclose the claimed invention individually, when considered in combination, the teachings of the references render the invention obvious. Applicant argues that it has not been explained why it would have been obvious to use the mutants of Beams in Souw's fusion proteins. However, as previously argued, Souw teaches the fusion of any HBV core antigen protein, or derivative thereof, including deletions thereof, to surface antigen epitopes. While Souw may not teach the exact fragment claimed in the instant application, it is clear that any HBV core protein fragment fused to the any fragment of surface antigen is taught (see pages 9-10 of Souw). Therefore, applicant's arguments are not convincing.

Claims 20, 22-25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nancy T. Vogel whose telephone number is (571) 272-0780. The examiner can normally be reached on 6:30 - 3:00, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone

number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

6/10/04

TERRY MCKELVEY
PRIMARY EXAMINER